REMARKS

Claims 1, 6, 24-29, 41, 69, 72-78, and 83-87 have been amended. Claim 93 and 94 have been added. Claims 44, 49, 50, 55, 56, 79-82, and 88-92 have been withdrawn. Therefore, claims 1, 6, 9-35, 37-41, 43, 44, 49, 50, 55, 56, 69, and 72-94 are pending in the case. Further examination and reconsideration of pending claims 1, 6, 9-35, 37-41, 43, 44, 49, 50, 55, 56, 69, and 72-94 are hereby respectfully requested.

Section 112, 2nd Paragraph, Rejections:

Claims 41, 78, and 83-84 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Office Action states that "The scope of the instant claims are ambiguous because the claims on its face uses the closed transitional phrase 'consisting of' in line 1 of the claim, but it further adds additional limitations in line 3 of the claims by reciting 'further consisting of one or more magnetic particles.'" (Office Action -- page 3.) Claims 41, 78, and 83-84 have been amended for clarification purposes. Applicant believes that the amendments to the claims address the Examiner's assertion of ambiguity in these claims. Accordingly, removal of the § 112, second paragraph, rejections of claims 41, 78, and 83-84 is respectfully requested.

Section 102 Rejections:

Claims 1, 9, 11, 14, 17, 21-23, 30-35, 37-38, 40, 73-75, and 85-86 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,288,502 to McGinity et al. (hereinafter "McGinity"). As will be set forth in more detail below, the § 102 rejections of claims 1, 9, 11, 14, 17, 21-23, 30-35, 37-38, 40, 73-75, and 85-86 are respectfully traversed.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987), MPEP § 2131. The cited art does not disclose all limitations of the currently pending claims, some distinctive limitations of which are set forth in more detail below.

The cited art does not teach a microcapsule consisting of internal, immiscible liquid phases enclosed within a polymer outer membrane, where a polymer of the polymer outer membrane does not extend from the polymer outer membrane into the microcapsule such that the liquid phases are not dispersed by the polymer. Amended independent claim 1 recites in part: "A microcapsule consisting of internal, immiscible liquid phases enclosed within a polymer outer membrane having a melting temperature, wherein a polymer of the polymer outer membrane does not extend from the polymer outer membrane into the microcapsule such that the liquid phases are not dispersed by the polymer." Amended independent claims 73-75 and 85-86 recite similar limitations. Support for the amendments to the claims can be found in the Specification and the Drawings, for example, FIG. 1A.

McGinity discloses preparation and uses of multi-phase microspheres. McGinity, however, does not disclose a microcapsule consisting of internal, immiscible liquid phases enclosed within a polymer outer membrane, where a polymer of the polymer outer membrane does not extend from the polymer outer membrane into the microcapsule such that the liquid phases are not dispersed by the polymer. For example, McGinity states that a method for preparing multi-phase microspheres includes

> mixing a biocompatible polymer and a polymer solvent together to form a polymer solution, dispersing the microemulsion into the polymer solution to form a W/O/'O' emulsion, mixing the W/O/'0' [sic] emulsion together in a dispersion oil which is incompatible with the polymer solvent to form a multiple emulsion, agitating and removing the solvent from the multiple emulsion to form hardened microspheres and washing and drying the hardened microspheres to form multi-phase microspheres containing the molecular compound. (McGinity -- col. 9, lines 1-11, emphasis added.)

McGinity also states that "These multi-phase microspheres include numerous, tiny microemulsions in the form of oily droplets dispersed throughout a biodegradable polymer matrix." (McGinity -- col. 12, lines 62-64, emphasis added.)

The biodegradable polymer matrix in which the microemulsions are dispersed are the same "wall polymers" disclosed in Table 1 of McGinity (McGinity -- col. 15, lines 40-51), which are cited as an "outer membrane polymeric shell" by the Examiner on page 4 of the Office Action. For example, McGinity specifically discloses that the "wall polymers," which include PLGA or PLA, also form the polymer matrix in which the microemulsions are dispersed. In particular, McGinity states that "PLA or PLGA are the preferred biodegradable polymers. Each of these polymers (about 3 grams) were first dissolved in a

volume of acetonitrile (about 4 grams, Fischer Scientific Co.). The W/O microemulsion (drug gelatin, Tween 80, Span 80, soybean oil, aluminum stearate) was poured int [sic] this polymer-acetonitrile solution and dispersed to form a W/O/'O' emulsion (multiple emulsion)." (McGinity -- col. 15, line 66 - col. 16, line 5.) In addition, McGinity states that in the same method "The multiple emulsion system was agitated by a stainless steel propeller for 24 hours to evaporate and remove the acetonitrile. The hardened microspheres were filtered using nylon screens." (McGinity -- col. 16, lines 14-18.) Therefore, the "outer membrane polymeric shell" and the biodegradable polymer matrix in which the microemulsions are dispersed are formed of the same polymer and in the same processing steps. Accordingly, the polymer of the "outer membrane polymeric shell" of McGinity extends from the "outer membrane polymeric shell" into the microspheres such that the microemulsions are dispersed by the polymer. McGinity further states that FIG. 11-A illustrates "Schematic features of a multi-phase microsphere (A) prepared by a multiple emulsion solvent evaporation technique." (McGinity -- col. 12, lines 33-35.) As shown in FIG. 11-A of McGinity, the "polymer wall" that forms the "outer membrane polymeric shell" extends from the "outer membrane polymeric shell" into the microcapsule such that the "polymer wall" disperses the water solution drugs in the W/O emulsion. As such, McGinity does not teach a microcapsule consisting of internal, immiscible liquid phases enclosed within a polymer outer membrane, where a polymer of the polymer outer membrane does not extend from the polymer outer membrane into the microcapsule such that the liquid phases are not dispersed by the polymer, as recited in claims 1, 73-75, and 85-86. Therefore, McGinity does not teach all limitations of claims 1, 73-75, and 85-86.

For at least the aforementioned reasons, claims 1, 73-75, and 85-86 are not anticipated by the cited art. Therefore, claims dependent therefrom are also not anticipated by the cited art for at least the same reasons. Accordingly, removal of the § 102 rejections of claims 1, 9, 11, 14, 17, 21-23, 30-35, 37-38, 40, 73-75, and 85-86 is respectfully requested.

Section 103(a) Rejections:

Claims 1, 6, 9-23, 26-35, 37-41, 43, 69, 72-78, and 83-87 were rejected under 35 U.S.C. § 103(a) as being unpatentable over McGinity in view of U.S. Patent No. 5,665,383 to Grinstaff et al. (hereinafter "Grinstaff"). Claims 1, 6, 9-35, 37-41, 43, 69, 72-78, and 83-87 were rejected under 35 U.S.C. § 103(a) as being unpatentable over McGinity in view of Grinstaff and further in view of U.S. Patent No. 5,985,312 to

Jacob et al. (hereinafter "Jacob"). As will be set forth in more detail below, the §103(a) rejections of claims 1, 6, 9-35, 37-41, 43, 69, 72-78, and 83-87 are respectfully traversed.

Jacob is not available as prior art against the present claims. As set forth in more detail above, claims 1, 6, 9-35, 37-41, 43, 69, 72-78, and 83-87 were rejected over a combination of Jacob and other cited art. As will be set forth in more detail below, Jacob is not usable as prior art against the present case since it has a priority date that is later than the priority date of the current application.

In particular, Jacob was filed on January 26, 1996. In contrast, the instant application is a continuation-in-part of U.S. Application No. 08/349,169 filed December 2, 1994, now U.S. Patent No. 5,827,531. Therefore, the priority date of the instant application is December 2, 1994. As such, the priority date of the instant application is earlier than the priority date of Jacob. Consequently, Jacob is not available as prior art against claims of the present application.

Since Jacob is not available as prior art for the current rejections, no combination of Jacob with other art may be used for the rejections of the present claims. Accordingly, removal of the § 103(a) rejections of claims 1, 6, 9-35, 37-41, 43, 69, 72-78, and 83-87 over Jacob in combination with other art is respectfully requested.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974), MPEP 2143.03. Obviousness cannot be established by combining or modifying the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion or incentive to do so. *In re Bond,* 910 F. 2d 81, 834, 15 USPQ2d 1566, 1568 (Fed. Cir. 1990). The remaining available cited art does not teach or suggest all limitations of the currently pending claims, some distinctive limitations of which are set forth in more detail below.

The remaining available cited art does not teach or suggest a microcapsule consisting of internal, immiscible liquid phases enclosed within a polymer outer membrane, where a polymer of the polymer outer membrane does not extend from the polymer outer membrane into the microcapsule such that the liquid phases are not dispersed by the polymer, as recited in claims 1, 73-75, and 83-87. As set forth in more detail above, McGinity does not teach all limitations of claims 1, 73-

75, and 83-87. Amended independent claims 41, 69, 72, 76-78, 83-84, and 87 recite similar limitations. Therefore, McGinity does not teach all limitations of claims 1, 41, 69, 72-78, and 83-87.

McGinity also does not suggest or provide motivation for all limitations of claims 1, 41, 69, 72-78, and 83-87. For example, modifying the invention of McGinity such that the polymer of the polymer outer membrane does not extend from the polymer outer membrane into the microcapsule such that the liquid phases are not dispersed by the polymer would render the prior art invention being modified unsatisfactory for its intended purpose. In particular, at least one intended purpose of the invention of McGinity is the constant and slow drug delivery from the microspheres. Furthermore, McGinity teaches that the constant and slow release rate is attributable to the biodegradable polymer matrix, which is formed of the polymer of the "outer membrane polymeric shell" that extends from the outer shell into the microspheres. For example, McGinity states that "The constant and slow rate of drug delivery may be attributable to the design of the multi-phase microspheres, which require that the molecular compound first traverse the water-oil barrier, and the polymer barrier of the polymer matrix, before the molecular compound/drug may diffuse out of the microsphere into the surrounding media or system (e.g., the system of an animal)." (McGinity -- col. 8, lines 5-12, emphasis added.) Similarly, McGinity states that "These multi-phase microspheres include numerous, tiny microemulsions in the form of oily droplets dispersed throughout a biodegradable polymer matrix. This technique innovatively provides for...enhancing the slow release characteristic of the compound from the microsphere." (McGinity -- col. 12, lines 62-68.) Again, McGinity states that "the unique 'microemulsion' design included in the claimed multi-phase microspheres provides for high water soluble molecule loading efficiency without loss of slow and constant control of drug release, as compared to the content-dependent rate of drug delivery observed in conventional microsphere systems." (McGinity -- col. 13, lines 14-20.)

Moreover, McGinity specifically states that the polymer matrix is part of the invention of McGinity. For example, McGinity states that "the delivery system of the present invention includes an aqueous molecular compound solution-in-oil emulsion of the water soluble molecular compound which comprises numerous tiny oily reservoirs within the polymer matrix of the multi-phase microsphere." (McGinity -- col. 7, lines 28-32.) McGinity also teaches that the polymer matrix provides several additional advantages over microspheres in the prior art. For example, McGinity states:

> the multi-phase microspheres disclosed herein were demonstrated to release the particular compounds incorporated therein at a rate independent of the particular molecular compound content of the microsphere. This important observation highlights one particular advantage of the present systems over those proposed in the literature, in that a constant and fixed rate of delivery of a molecular compound is provided without sacrificing high drug loading efficiency in the microsphere. (McGinity -- col. 7, line 60 - col. 8, line 1.)

In addition, McGinity states that "The basic technological breakthrough provided with the present disclosure may be applied in preparing slow-release, long-acting, multi-phase microspheres with virtually any micro- or macromolecule, including synthetic, potent proteins and peptides. Thus, the proposed compositions and methods present a highly cost effective and therapeutically valuable delivery system." (McGinity -- col. 5, lines 46-52.) Furthermore, McGinity states that "the slow release action of the presently disclosed multi-phase microspheres make possible the design of in vivo treatment regimens which are effective over therapeutically valuable and/or necessary treatment periods." (McGinity -- col. 13, lines 8-12).

As a result, since the polymer matrix of McGintiy is formed of a portion of the "outer membrane polymeric shell" that extends from the outer shell into the microspheres, the "outer membrane polymeric shell" of McGinity cannot be modified such that the polymer of the "outer membrane polymeric shell" does not extend from the outer shell into the microspheres. For example, if the microspheres of McGinity were so modified, there would be a single layer of biodegradable material surrounding the material to be delivered. As such, the contents of the microspheres would not be delivered until at least a portion of the outer shell biodegrades sufficiently at which point an entirety of the contents of the microspheres would be delivered. Therefore, the delivery rate of the modified microspheres of McGinity would be variable and quick. Consequently, since the purpose of the invention of McGinity is the constant and slow delivery of drugs from microspheres, such modifications of the microspheres of McGinity would render the prior art invention unsatisfactory for its intended purpose. Therefore, there is no suggestion or motivation to modify McGinity or to combine McGinity with any other art such that all limitations of the claims are taught. If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). MPEP 2143.01.

Furthermore, the teachings of McGinity appear to lead away from the presently claimed invention. For example, as set forth in more detail above, the teachings of McGinity lead away from a polymer outer

membrane, where a polymer of the polymer outer membrane does not extend from the polymer outer membrane into the microspheres since such a modification would prevent the polymer matrix as taught by McGinity to be formed. In particular, the elimination of the polymer matrix from the biodegradable microspheres of McGinity would cause the delivery rate of the microspheres to be variable and quick since, as set forth in more detail above, such modifications would cause the entire contents of the microspheres to be released substantially simultaneously. Therefore, multiple injections would be required to treat an animal over any period of time, which is obviously disadvantageous. In addition, McGinity specifically states that eliminating multiple injections is an advantage of the invention of McGinity (McGinity -- col. 13, lines 12-14). A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). MPEP 2141.02.

For at least the reasons provided above, McGinity does not suggest the desirability of the limitations of the present claims. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). MPEP 2143.01. Therefore, even if McGinity could be combined or modified to teach the limitations of the present claims, the resultant combinations or modifications are not obvious since the prior art clearly does not suggest the desirability of such combinations or modifications.

For example, McGinity cannot be combined with Grinstaff to overcome the deficiencies therein. Grinstaff discloses methods for the preparation of immunostimulating agents for in vivo delivery. In particular, Grinstaff states that "Invention compositions comprise biologic (as a solid, liquid or gas) associated with a polymeric shell. The polymeric shell is a biocompatible material, crosslinked by the presence of disulfide bonds." (Grinstaff -- col. 6, lines 11-14.) Therefore, even if Grinstaff taught a polymeric shell that could be considered equivalent to the claimed polymer outer membrane, the teachings of McGinity cannot be modified by Grinstaff for at least the reasons set forth above. Consequently, the combination of McGinity and Grinstaff does not teach a microcapsule consisting of internal, immiscible liquid phases enclosed within a polymer outer membrane, where a polymer of the polymer outer membrane does not extend from the polymer outer membrane into the microcapsule such that the liquid phases are not

dispersed by the polymer, as recited in claims 1, 41, 69, 72-78, and 83-87. As such, the cited art does not teach, suggest, or provide motivation for all limitations of claims 1, 41, 69, 72-78, and 83-87.

For at least the reasons stated above, claims 1, 41, 69, 72-78, and 83-87 are patentably distinct over the cited art. Therefore, claims dependent therefrom are also patentably distinct over the cited art for at least the same reasons. Accordingly, removal of the § 103(a) rejections of claims 1, 6, 9-35, 37-41, 43, 69, 72-78, and 83-87 is respectfully requested.

Patentability of the Added Claims:

The present amendment adds claims 93-94, which are dependent from claim 1. Therefore, claims 93-94 are patentable over the cited art for at least the same reasons set forth above. Accordingly, allowance of claims 93-94 is respectfully requested.

CONCLUSION

This response constitutes a complete response to all issues raised in the Office Action mailed March 24, 2004. In view of the remarks traversing rejections presented therein, Applicants assert that pending claims 1, 6, 9-35, 37-41, 43, 44, 49, 50, 55, 56, 69, and 72-94 are in condition for allowance. If the Examiner has any questions, comments, or suggestions, the undersigned earnestly requests a telephone conference.

The Commissioner is authorized to charge any required fees or credit any overpayment to Deposit Account No. 14-0116.

Respectfully submitted,

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